REMARKS/ARGUMENTS

In a non-final Office Action mailed December 3, 2003, the Examiner in charge of the application rejected pending Claims 5-7, 11-13 and 19-21 as anticipated by WO200134626-A1 (Accession No. AAD5303), Accession No. BC012074 from NCBI. The Examiner further rejected Claims 5-7 under 35 U.S.C. §102(a) or (b) as being anticipated by St. Croix et al. (2000).

Each issue raised by the Examiner is considered separately below. In view of the amendments noted above and the arguments below, applicants respectfully request reconsideration of the merits of this patent application.

Rejections Under 35 U.S.C. §102(a) based on WO200134626-A1 and BC012074

The Examiner alleged that WO200134626-A1 and BC012074 disclose SEQ ID NO:1 (polynucleotide sequence) and SEQ ID NO:2 (amino acid sequence encoded by SEQ ID NO:1) of the present invention. The Examiner further alleged that the polypeptide sequences disclosed in WO200134626-A1 and BC012074 are inherently soluble and thus anticipate the pending claims. Applicants respectfully disagree.

To anticipate the pending claims, WO200134626-A1 and BC012074 must disclose all limitations in the pending claims. As Applicants detail below, the cited patent application and nucleic acid sequence cannot anticipate the claims because neither discloses the soluble and PA-binding limitations recited in the claims.

1. The pending claims relate only to a limited number of SEQ ID NO:2 fragments.

Independent Claims 5 and 19 recite a soluble and PA-binding fragment of SEQ ID NO:2. Only a limited number of fragments of SEQ ID NO:2 are soluble and PA-binding.

As the application describes at paragraph [00027], the protein defined by SEQ ID NO:2 (368 amino acids long) contains a signal peptide (amino acids 1-27), an extracellular domain (amino acids 28-320), a transmembrane domain (amino acids 320-343) and a cytoplasmic domain (amino acids 344-368). It is well known in the art that a protein with a hydrophobic transmembrane domain is insoluble. In fact, amino acids 320-343 of SEQ ID NO:2 is identified as a transmembrane domain precisely because it is hydrophobic and shares a high degree of homology to other hydrophobic transmembrane domains. By limiting the SEQ ID NO:2 fragments to soluble fragments, a skilled artisan understands that the fragments

in the pending claims cannot contain a substantial part of the transmembrane domain. For example, the application describes soluble fragments of SEQ ID NO:2 that end at amino acid 321, part of the junction region between the extracellular domain and the transmembrane domain. See paragraph [00035] of the application.

A skilled artisan would also understand that a limitation to a PA-binding fragments of SEQ ID NO:2 (anthrax toxin receptor) in the pending claims excludes very short fragments. It is well established in the art that a cellular membrane receptor binds its ligand through a ligand binding motif in the extracellular domain. The skilled artisan likewise appreciates that while the whole ligand binding motif or extracellular domain is not always required for ligand binding, too short a fragment cannot retain ligand binding activity. The present application discloses in paragraph [00033] how to use routine experimentation to determine whether a fragment is PA-binding. Further, examples of PA-binding fragments are provided in the application. See paragraph [00035].

In summary, the pending claims only relate to SEQ ID NO:2 fragments that are soluble and PA-binding.

2. *WO200134626-A1 discloses a full length protein that contains a transmembrane domain, a secreted protein, and any fragments of the full length protein. However, none of these anticipates the soluble and PA-binding fragments in the pending claims.*

WO200134626-A1 discloses a protein that contains 403 amino acids (SEQ ID NO:94 and SEQ ID NO:125). WO200134626-A1 further discloses that the protein defined by SEQ ID NO:94 and SEQ ID NO:125 contains a signal peptide (amino acids 1-27), a transmembrane domain (amino acids 322-338), and a cytoplasmic tail (amino acids 339-403). See Table 1 on pages 67 and 68 and lines 22-25 of page 12 of WO200134626-A1. SEQ ID NO:14 and SEQ ID NO:45 disclose the nucleotide sequences that encode the amino acid sequences of SEQ ID NO:94 and SEQ ID NO:125, respectively. Since SEQ ID NO:94 and SEQ ID NO:125 are the same sequence except that SEQ ID NO:94 further identifies the 4 undetermined amino acids in SEQ ID NO:125 (amino acids 175, 320, 331, and 368, labeled as Xaa), the discussion below, while applicable to both SEQ ID NO:94 and SEQ ID NO:125, makes reference only to SEQ ID NO:94 for conciseness

For the convenience of the Examiner, SEQ ID NO:94 and SEQ ID NO:125 of

WO200134626-A1 and SEQ ID NO:2 of the present invention are enclosed as Exhibit A. The first 363 amino acids of SEQ ID NO:94 match the first 363 amino acids of SEQ ID NO:2 in the present application.

The disclosure of the whole protein as defined by SEQ ID NO:94 does not anticipate the present invention because the whole protein contains the full length transmembrane domain which makes the protein insoluble, whereas the pending claims recite a soluble, PA-binding fragment of SEQ ID NO:2.

Further, the disclosure of a secreted protein in WO200134626-A1, as in claim 2 in particular, does not anticipate the soluble, PA-binding fragment of SEQ ID NO:2 in the pending claims because a secreted protein cannot be equated with a soluble protein. Rather, reference must be had to the cited application to determine the definition of the disclosed secreted protein.

WO200134626-A1 defines a secreted protein as a protein capable of being directed to the ER, secretory vesicles, or the extracellular space. See lines 1-3 on page 3. Since a signal sequence at the N-terminus of the protein confers this capability on the protein, and since the signal sequence is cleaved from the protein in an initial processing step, a secreted protein of WO200134626-A1 can only refer to a protein in a nascent, unprocessed form. See page 91, line 29 to page 92, line 11. The protein is no longer capable of being directed the ER, secretory vehicles, or the extracellular space after cleavage of the signal peptide.

The protein of SEQ ID NO:94 cannot be directed to secretory vesicles or the extracellular space because it is a membrane protein having a transmembrane domain. On the other hand, the signal peptide can direct the protein to the ER for translocation to the cellular membrane (amino acids 1-27, see Table 1 on page 68 of WO200134626-A1). Therefore, a secreted protein capable of being directed to the ER necessarily refers to the full-length 403-amino acid long protein of SEQ ID NO:94, including the transmembrane domain. Under this definition, the secreted protein defined by SEQ ID NO:94 is not soluble and cannot anticipate the soluble, PA-binding fragment of SEQ ID NO:2 in the pending claims.

WO200134626-A1 further states that a secreted protein can also be a protein released into the extracellular space. See lines 1-3 on page 3 of WO200134626-A1. As noted above, this cannot apply to the proteins at issue because the proteins of SEQ ID NO:2 of the present application and SEQ ID NO:94 of WO200134626-A1 are membrane proteins and are not released into the extracellular space. It is noted that WO200134626-A1 discloses many other proteins that can be released into the extracellular space. Therefore, by this definition,

WO200134626-A1 refers to the other proteins but not that of SEQ ID NO:94.

Finally, the disclosure of fragments of proteins in WO200134626-A1, including fragments of SEQ ID NO:94, cannot anticipate the soluble, PA-binding fragments of SEQ ID NO:2 in the pending claims. The fragments of SEQ ID NO:Y in claim 1(b) and claims 3-4 of WO200134626-A1 are not limited in any way and thus encompass all fragments of SEQ ID NO:Y. The specification does not limit the fragments either. See page 3, line 25 of WO200134626-A1. No specific fragments of SEQ ID NO:94 are described in WO200134626-A1. A skilled artisan understands that not all fragments of SEQ ID NO:94 are soluble and capable of binding to PA.

The soluble, PA-binding fragments of SEQ ID NO:2 in the pending claims are only species of the broad "all fragments of SEQ ID NO:94" genus as disclosed in WO200134626-A1. The "soluble" and "PA-binding" limitations that further define the species are lacking from the broad genus disclosure of WO200134626-A1. Therefore, WO200134626-A1 cannot anticipate the pending claims.

The Examiner alleged that the use of the partially closed transitional phrase "consisting essentially of" in the pending claims makes WO200134626-A1 appear to anticipate the claims. Although applicants do not agree with the Examiner, in order to expedite the present application to allowance, applicants have amended Claims 5 and 19 so that the polynucleotides recited therein encode only soluble polypeptides. For the reasons discussed above, the pending claims so amended are not anticipated by WO200134626-A1.

3. *The "soluble" property is not inherent in the polypeptides disclosed in WO200134626-A1.*

The Examiner alleged that it is inherent that the sequences disclosed in WO200134626-A1 are soluble since the cited application discloses the same or similar sequences as SEQ ID NO:1 and 2 of the present application. Applicants respectfully disagree.

In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). Here, the allegedly inherent characteristic (solubility) does not necessarily flow from the teachings of the applied art.

First, the full length of SEQ ID NO:94 is clearly not soluble because it contains the transmembrane domain. Second, the fragments of SEQ ID NO:94 as disclosed in WO200134626-A1 are not limited in any way and thus encompass all fragments of SEQ ID NO:94. A skilled artisan appreciates that not all fragments of SEQ ID NO:94 are soluble. For example, fragments that contain the full length transmembrane domain are not soluble. Since many fragments of SEQ ID NO:94 are not soluble it is not accurate to state that the full length protein or a fragment thereof as disclosed in WO200134626-A1 is inherently soluble.

4. WO200134626-A1 does not render the soluble, PA-binding fragments of SEQ ID NO:2 in the pending claims obvious.

The Examiner alleged that since WO200134626-A1 discloses the same or similar sequences as SEQ ID NO:1 and 2 of the present application, it renders the soluble, PA-binding fragment of SEQ ID NO:2 in the pending claims obvious. Applicants respectfully disagree.

For WO200134626-A1 to render the pending claims obvious, the document must provide some explicit or implicit suggestion to make a soluble, PA-binding fragment of SEQ ID NO:94. Such suggestion is lacking. WO200134626-A1 discloses the full length protein defined by SEQ ID NO:94 as well as any fragment thereof. There is no suggestion to make a soluble, PA-binding fragment of the sequence.

The present case falls within the "genus-species" scenario. When a prior art reference discloses a genus, claims directed at certain species of the genus that are advantageous over other species of the genus are patentable if the prior art reference does not specifically disclose the species and does not recognize the advantages. WO200134626-A1 discloses all fragments of SEQ ID NO:94 as a genus, including soluble and insoluble fragments and PA-binding and non-PA-binding fragments. In contrast, the pending claims are directed at certain exemplified species of the genus, namely, those fragments that are soluble and PA-binding. The present invention recognizes the advantages of the soluble and PA-binding fragments as being able to compete with an anthrax toxin for binding to its receptors. Therefore, the pending claims are patentable over WO200134626-A1.

5. BC012074 does not anticipate the pending claims.

BC012074 encodes a protein with 334 amino acids, the first 317 of which are identical to those of SEQ ID NO:2 of the present application. However, the protein encoded by BC012074 differs from SEQ ID NO:2 of the present invention after amino acid 317. BC012074 does not disclose any sequence fragments. Since BC012074 only discloses a DNA sequence that encodes the whole protein, which differs from the protein defined by SEQ ID NO:2 of the present invention by at least 17 amino acids, BC012074 does not anticipate the present invention. An alignment analysis conducted by the undersigned is enclosed as Exhibit B. The alignment shows that when SEQ ID NO:1 of the present invention and BC012074 were aligned, only nucleotides 1-1054 of SEQ ID NO:1 encoding amino acids 1-317 and nucleotides 10-1063 of BC012074 encoding amino acids 1-317 demonstrated identity/similarity.

Rejections Under 35 U.S.C. §102(a) or (b) based on St. Croix et al. (AF279145)

St. Croix et al. disclose a DNA sequence (AF279145) that encodes a protein of 565 amino acids, the first 363 of which are the same as those of SEQ ID NO:2 of the present invention. An alignment analysis conducted by the undersigned is enclosed as Exhibit C. The alignment shows that when SEQ ID NO:1 of the present invention and AF279145 were aligned, only nucleotides 1-1192 of SEQ ID NO:1 encoding amino acids 1-363 and nucleotides 41-1232 of AF279145 encoding amino acids 1-363 demonstrated identity/similarity.

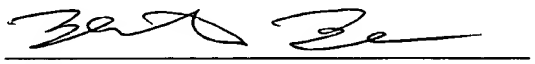
The protein encoded by AF279145 contains a transmembrane region (amino acids 320-343). See GenBank database for AF279145. Thus, the protein encoded by AF279145 is not soluble. Since St. Croix et al. only disclose the DNA sequence that encodes an insoluble full length protein but not a soluble and PA-binding fragment, St. Croix et al. do not anticipate the pending claims or render the pending claims obvious, for the same reasons discussed in connection with WO200134626-A1.

Having responded to each ground of rejection imposed by the Examiner, applicants respectfully request reconsideration of the merits of this patent application.

A petition for an extension of time for one month accompanies this response so the response will be deemed to have been timely filed. Should any additional extension of time

be due, please consider this to be a request for the appropriate extension of time and a request to charge the required fee to Deposit Account No. 17-0055. No other fee is believed due, but should any other fee be due, please consider this to be a request to charge the fee to the same Deposit Account.

Respectfully submitted,



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